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) OFFICE (DO/EO/US) U.S. APPLICATION NO. (If known, see 37 CFR 1.5)
UNDER 35 U.S.C. 371

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP 99/06572	9 September 1999	9 September 1998

TITLE OF INVENTION: METHOD AND DEVICE FOR PRODUCING TABLETS

APPLICANT(S) FOR DO/EO/US Joerg ROSENBERG, Karl Ludwig JOTTER, Werner MAIER, Burkhard TRAPP, Klaus TSCHOCHNER

THE US PATENT & TRADEMARK OFFICE
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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. /X/ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.

2. / / This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.

3. /X/ This express request to begin national examination procedures (35 U.S.C.371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. /x / A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. /X/ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).

   a./X/ is transmitted herewith (required only if not transmitted by the International Bureau).
   b./ / has been transmitted by the International Bureau.
   c./ / is not required, as the application was filed in the United States Receiving Office (RO/US0).

6. /X/ A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. / / Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).

   a./ / are transmitted herewith (required only if not transmitted by the International Bureau).
   b./ / have been transmitted by the International Bureau.
   c./ / have not been made; however, the time limit for making such amendments has NOT expired.
   d./ / have not been made and will not be made.

8. / / A translation of the amendments to the claims under PCT Article 19(35 U.S.C. 371(c)(3)).

9. /X / An oath or declaration of the inventor(s)(35 U.S.C. 171(c)(4)).

10./ / A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11./ / An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12./X / An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13./X / A FIRST preliminary amendment.
/ / A SECOND or SUBSEQUENT preliminary amendment.

14./ / A substitute specification.

15./ / A change of power of attorney and/or address letter.

16./x / Other items or information.
International Search Report
International Preliminary Examination Report

09/787079

JC08 Rec'd PCT/PTO 07 MAR 2001

U.S. Appln. No. (If Known)	INTERNATIONAL APPLN. NO. PCT/EP99/06672	ATTORNEY'S DOCKET NO. 0480/001216

17. /X/ The following fees are submitted	CALCULATIONS	PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO.....$860.00	860.00	
International preliminary examination fee paid to USPTO (37 CFR 1.482).....$750.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but International search fee paid to USPTO (37 CFR 1.445(a)(2)).....$700.00		
Neither international preliminary examination fee (37 CFR 1.482) nor International search fee (37 CFR 1.445(a)(2)) paid to USPTO .....$ 970.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied pro -visions of PCT Article 33(2)-(4).....$96.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 860.00	
Surcharge of $130.00 for furnishing the oath or declaration later than / / 20 / /30 months from the earliest claimed priority date (37 CFR 1.492(e)).		

Claims	Number Filed	Number Extre	Rate	
Total Claims	11	-20	X$18.	
Indep.Claims	1	-3	X$80.	
Multiple dependent claim(s)(if applicable)		+270.		
TOTAL OF ABOVE CALCULATION			= 860.00	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).				
SUBTOTAL			= 860.00	
Processing fee of $130. for furnishing the English translation later than / /20 / /30 months from the earliest claimed priority date (37 CFR 1.492(f)).		+		
TOTAL NATIONAL FEE			= **860.00**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) $40.00 per property		=	40.00	
TOTAL FEES ENCLOSED			= $ **900.00**	
		Amount to be refunded:	$	
		Charged	$	

a./X/ A check in the amount of $ 900. to cover the above fees is enclosed.

b./ / Please charge my Deposit Account No._____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c./X/ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. **11-0345**. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

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09/787079
JC08 Rec'd PCT/PTO 07 MAR 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of)
ROSENBERG et al.) BOX PCT
)
International Application)
PCT/EP 99/06672)
)
Filed: September 9, 1999)
)

For: METHOD AND DEVICE FOR PRODUCING TABLETS

PRELIMINARY AMENDMENT

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-identified application as follows:

IN THE CLAIMS

3. A process as claimed in claim 1 [either of claims 1 or 2], wherein a force with a component parallel to the plane of the tablet belt is allowed to act on the tablet belt for singulation of the tablets.

4. A process as claimed in claim 2 [either of claims 2 or 3], wherein the perpendicular force component is generated by diverting the solidified tablet belt out of its transport plane.

5. A process as claimed in claim 3 [either of claims 3 or 4], wherein the parallel force component is generated by exerting a traction force on the solidified tablet belt.

7. An apparatus as claimed in claim 6, wherein the singulating means [(40)] comprises at least one rotatable roller [(41)] for diverting the tablet belt [(14)] out of a transport plane [(34)] of the first transport means [(30)].

8. An apparatus as claimed in claim 7, wherein the singulating means [(40)] comprises two counter-rotating rollers [(41, 42)] which can be pressed against one another.

9. An apparatus as claimed in claim 6 [any of claims 6 to 8], wherein the singulating means [(40)] comprises at least one brush roller or embossed roller [(41)].

10. An apparatus as claimed in claim 6 [any of claims 6 to 9], wherein the first transport means [(30)] comprises means [(70)] for cooling the extruded tablet belt.

11. An apparatus as claimed in claim 6 [any of claims 6 to 10], wherein a second transport means [(60)] is provided between the singulating means [(40)] and the deflashing means

[(50)] and comprises a shaking or vibrating unit [(61)].

Cancel claim 6 and insert new claim 12 as follows:

--12. An apparatus for producing tablets, comprising

at least one extruder,

means for shaping a tablet belt arranged downstream of said extruder,

first transport means for said tablet belt arranged downstream of said shaping means, and

means for singulating and deflashing said tablets, wherein said means for singulating and deflashing said tablets comprise at least one singulating means arranged downstream of said first transport means, and at least one deflashing means arranged downstream of said singulating means and spatially separate therefrom.--

REMARKS

The claims have been amended to eliminate multiple dependency and to put them in better form for U.S. filing. No new matter is included. A clean copy of the claims is attached.

Favorable action is solicited.

Respectfully submitted,

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CLEAN COPY OF CLAIMS FOR OZ 0480/001216

1. A process for producing tablets by melt extrusion, in which an extrudable mixture is heated and extruded in the form of a continuous product strip, the still deformable product strip is compressed to a continuous tablet belt, the individual tablets in the belt being connected together by product webs, the tablet belt is allowed to cool, and the tablets are finally singulated and deflashed, wherein firstly the tablets are mechanically singulated in a continuous process, and then the singulated tablets are transported further and subsequently deflashed.

2. A process as claimed in claim 1, wherein a force with a component perpendicular to the plane of the tablet belt is allowed to act on the tablet belt for singulation of the tablets.

3. A process as claimed in claim 2, wherein a force with a component parallel to the plane of the tablet belt is allowed to act on the tablet belt for singulation of the tablets.

4. A process as claimed in claim 2, wherein the perpendicular force component is generated by diverting the solidified tablet belt out of its transport plane.

5. A process as claimed in claim 3, wherein the parallel force component is generated by exerting a traction force on the solidified tablet belt.

CLAIM 6 HAS BEEN CANCELED

7. An apparatus as claimed in claim 6, wherein the singulating means comprises at least one rotatable roller for diverting the tablet belt out of a transport plane of the first transport means.

8. An apparatus as claimed in claim 7, wherein the singulating means comprises two counter-rotating rollers which can be pressed against one another.

9. An apparatus as claimed in claim 6, wherein the singulating means comprises at least one brush roller or embossed roller.

10. An apparatus as claimed in claim 6, wherein the first transport means comprises means for cooling the extruded tablet belt.

11. An apparatus as claimed in claim 6, wherein a second transport means is provided between the singulating means and the deflashing means and comprises a shaking or vibrating unit.

12. An apparatus for producing tablets, comprising

at least one extruder,

means for shaping a tablet belt arranged downstream of said extruder,

first transport means for said tablet belt arranged downstream of said shaping means, and

means for singulating and deflashing said tablets, wherein said means for singulating and deflashing said tablets comprise at least one singulating means arranged downstream of said first transport means, and at least one deflashing means arranged downstream of said singulating means and spatially separate therefrom.

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2/PRTS

JC08 Rec'd PCT/PTO 07 MAR 2001

Process and apparatus for producing tablets

The present invention relates to a process and an apparatus for producing tablets by melt extrusion.

European patent EP-B-0 240 906 discloses a process for producing tablets by melt extrusion, in which an extrudable pharmaceutical mixture is heated and extruded in the form of a continuous product strip, the product strip which is still moldable is compressed to a continuous tablet belt, the individual tablets in the belt being connected together by product webs, the tablet belt is allowed to cool, and the tablets are finally singulated and deflashed.

In contrast to conventional processes which are based on the compression of powders or granules, in the melt extrusion process an active ingredient-containing melt of a thermoplastic, water-soluble or water-swellable polymer is processed.

For this purpose, the individual components are first mixed and then melted in an extruder. The mixing of the components may also take place in the extruder. Suitable extruders are, for example, single screw machines, intermeshing screw machines, multiscrew extruders, especially twin screw extruders, which may be designed to be corotating or counter-rotating and, where appropriate, may be equipped with kneading disks. Suitable extruders are included, for example, in the ZSK series from Werner & Pfleiderer.

The extruder may have a plurality of inlets. It is possible, where appropriate, to provide separate addition of solid and liquid ingredients of the mixture. It is additionally possible to provide connectors for introducing inert gas and/or for degassing. Since the mixing of the ingredients takes place in the extruder, it is normally possible to dispense with premixing. The heated pharmaceutical mixture is expelled in the form of product strips or belts through one or more dies, for example slit dies, in the extruder head. The product strips or belts are then sent to shaping means. Various means for shaping tablets from active ingredient-containing melts are known. For example, the melt can be compressed to tablets by a calendering process using counter-rotating molding rolls. In this case, depressions corresponding to the desired tablet shape are provided in one or in both molding rolls. However, it is also possible to allow a belt having depressions or apertures of the desired tablet shape to pass through between two smooth calender rolls. The tablet belt produced by calendering contains the shaped individual

tablets, which are normally connected together by fine burrs or product webs. These product webs may in fact be useful in the shaping because they favor release of the tablet from the mold. Concerning the procedure for the conventional melt extrusion process, reference may be made not only to EP-B-0 240 906 but also to EP-B-0 240 904, EP-B-0 337 256 and EP-B-0 358 105.

To produce single tablets from the tablet belt shaped in this way, the belt is initially allowed to cool, and the cooled tablet belts are put into a large vessel, which is made to rotate. The mechanical stress arising thereby, which can be controlled within certain limits by the quantity of tablets added, the size of the vessel and its speed of rotation, leads to singulation of the large, plate-like parts of the tablet belt stepwise to ever smaller aggregates, until finally only a large proportion of so-called "twins" still remains, which is singulated to individual tablets as the process continues. Collision of the tablets during rotation in the vessel abrades off the residues of the burrs, so that the tablets are also deflashed simultaneously with the singulation.

The known process for producing single tablets by melt extrusion is, however, associated with disadvantages. Whereas the melt extrusion process provides a continuous process for producing tablets, the final singulation and deflashing process takes place batchwise in vessels. Since the processing time in the vessel, in particular for singulating the tablets from the tablet belt, is relatively long, the possible productivity of a continuous tablet production by melt extrusion is not exploited. In addition, it has emerged that this simple singulation and deflashing process in the vessel is not successful in all cases. In the particular case of tablets having a score to facilitate dividing, the known process leads to a high proportion of broken tablets, which must be rejected mechanically and considerably reduce the yield. Divisible tablets having a score have, however, in recent years become increasingly frequently employed because it is possible with them to adapt the dose, e.g. pediatric/adult dosage, with a single tablet.

It is an object of the present invention to provide a process for producing tablets by melt extrusion which firstly makes greater productivity possible and, moreover, ensures production of tablets which are easily broken, for example divisible tablets, without unacceptably high loss rates. Another object of the present invention is to provide an apparatus for carrying out the process.

We have found that this object is achieved by the process claimed in the main claim herein.

The present invention accordingly relates to a process for producing tablets by melt extension in which, in a manner known per se, an extrudable, preferably pharmaceutical, mixture is heated and extruded in the form of a continuous product strip, the still deformable product strip is compressed to a continuous tablet belt, the individual tablets in the belt being connected together by product webs, the tablet belt is allowed to cool, and the tablets are finally singulated and deflashed, wherein firstly the tablets are mechanically singulated in a continuous process, and then the singulated tablets are transported further and subsequently deflashed.

Accordingly, the invention proposes that the combined singulation and deflashing process which in known processes takes place in a cylindrical vessel be carried out in two separate steps, with the singulation process taking place continuously.

The process of the invention is associated with numerous advantages. A continuous singulation of the tablet belt to single tablets means that this step can take place at the same speed as the shaping of the tablets by melt extrusion. The subsequent deflashing step can take place in a vessel as in the process of the invention. Preference is given to employment of coating vessels known per se or machines used for film coating (for example the Dria-Coater from Driam). Since it is no longer necessary for singulation to take place in the vessel, the time required for deflashing therein is distinctly reduced. The overall result therefore is a saving in processing time compared with the known process.

The separation, provided according to the invention, of singulation and deflashing additionally allows the two processes to be specifically adapted to particular requirements. Since it is now necessary in the concluding deflashing step in the vessel only to remove the residues of the burr present on the individual tablets, the deflashing can be carried out under milder conditions. In the prior art process, the energy input into the vessel is considerably greater, because it is also necessary in particular for the singulation of the larger tablet plates to take place therein. The process of the invention can therefore be employed with particular advantage in particular in the production of tablets which break easily, such as, for example, tablets with scores.

For singulation of the tablet belt by the process of the invention it is necessary to reduce the temperature of the tablets until there is no bending or deformation of the tablets, which may still be plastic, on exposure to a mechanical force.

In an advantageous embodiment of the process of the invention, a force with a component perpendicular to the plane of the cooled tablet belt is allowed to act on the belt to singulate the tablets. This leads directly to a bending and subsequent breaking of the tablet belt at the thin product webs which connect the individual tablets together. The process functions very efficiently in particular when the temperature of the tablet belt is low enough for the thin product webs or burrs no longer to be plastic, but to display a certain brittleness. However, it is also possible to allow a force to act in the plane of the tablet belt, so that the tablets are torn apart at the product webs. This variant of the process of the invention can even be employed when the temperature of the tablet belt is still high enough for the product webs still to have a certain plasticity. However, a particularly advantageous process is one in which there is both a force acting perpendicular to the tablet belt and a force acting in the plane of the tablet belt.

The perpendicular component of force is preferably generated by diverting the solidified tablet belt out of its transport plane, while the parallel component of force is generated by exerting a traction force on the solidified tablet belt.

The present invention also relates to an apparatus for producing tablets, in particular for carrying out the process of the invention described above. The apparatus of the invention comprises at least one extruder, means, downstream of the extruder, for shaping a tablet belt, first transport means, downstream of the shaping means, for the tablet belt and means for singulating and deflashing the tablets. In the apparatus of the invention, the means for singulating and deflashing the tablets comprise at least one singulating means, arranged downstream of the first transport means, and at least one deflashing means, arranged downstream of the singulating means and spatially separate therefrom. Suitable shaping means are primarily two molding rolls which can be pressed against one another, as described in the European patent EP-B-0 240 906 mentioned at the outset. The first transport means may be, for example, a conveyor belt which serves primarily for cooling the pharmaceutical melt which has been compressed to a tablet belt.

The singulating means following the first transport means is particularly advantageously designed as roller arrangement. In a simple embodiment, the singulating means comprises at least one rotatable roller for diverting the tablet belt out of a transport plane of the first transport means. The melt, which is initially still plastic, solidifies on the first transport means so that the solidified tablet belt leaves the transport means in a plane defined by the latter. It is possible to arrange a rotatable roller immediately following the transport means, which roller diverts the rigid belt for example downwards and thus exerts the force, provided in the process of the invention, perpendicular to the table belt. This diversion is associated with breakage of the, now brittle, connecting webs between the tablets. In an advantageous embodiment of the apparatus of the invention, the singulating means is designed as two counter-rotating rollers which can be pressed against one another. One of the rollers rotates above and the other roller rotates beneath the tablet belt. The rollers can be designed to be driveable. The speed of rotation can be selected to be greater than the speed with which the tablet belt is transported on the first transport means, so that the rollers generate a traction force in the plane of the tablet belt. The rollers can be arranged so that the tangential plane of the slot through which the tablet belt passes forms an angle with the plane of the tablet belt on the transport means, so that once again diversion of the solidified belt is brought about, leading to breakage of the tablet belt at the product webs. The rollers or roller combinations used as singulating means can easily be adapted to the different requirements of specific tablet formulations. For example, it is possible to employ rollers differing in surface structure. It is possible to use, for example, smooth rollers, rollers with brushes or pins, with bars or other structures. The force applied for the singulation can be influenced by changing the arrangement of the rollers, the diameter of the rollers and the contact pressure. Other possibilities are different combinations of material, for example foams, plastics, rubber or stainless steel. It is possible in particular to influence the traction force in the plane of the tablet belt through the speed of rotation of the rollers.

In a preferred embodiment of the invention, the first transport means has additional means for cooling the extruded and shaped tablet belt. If the transport means is designed, for example, as circulating conveyor belt it is possible to provide one or more cooling plates underneath the upper part of the belt. The cooling can be adapted to the specific requirements of the particular tablet formulation through the length of the transport belt. With

longer transport belts it is possible to divide the cooling section into individual zones which are cooled separately, so that a stepwise, easily controlled cooling process can be carried out.

The cooling provided for the first transport means can, however, also take place by air cooling. In this case, cooling from above is possible, for example with cooling air being allowed to pass over the shaped tablet belt. However, it is also possible to design the transport belt with perforations and provide air cooling from below. Cooling of the tablet belt can, however, also take place, for example, by spraying with cooling water.

In a particularly preferred embodiment of the apparatus of the invention, a second transport means is provided between the singulation means and the deflashing means and comprises a shaking or vibrating unit. The latter can be designed, for example, as vibrating screen. After the singulation, the tablets fall onto a vibrating screen and are transported thereon to the deflashing means. Larger residues of the burrs are removed from the tablets even on the vibrating screen, so that the processing time for the deflashing is further reduced. It is also possible for any "twins" still present after the singulation, that is to say two tablets still connected by product webs, to be separated on the vibrating second transport means.

The present invention is explained in more detail below with reference to an example depicted in the drawings attached.

The drawings show:

Figure 1 a diagrammatic representation of an apparatus of the invention for producing single tablets by melt extrusion;

Figure 2 a plan view of a tablet belt immediately after shaping with the molding calender rolls; and

Figure 3 a section through the tablet belt of Fig. 2;

Figure 4 a plan view of a variant of the roller arrangement of the singulating means;

Figure 5 a plan view of another embodiment of the breaking roller of the singulating means.

Figure 1 depicts an overall view of a preferred embodiment of the apparatus of the invention. The extruder 10, which is depicted diagrammatically, serves to mix and melt the pharmaceutical mixture. An extruder head 11 of the extruder 10 has a slit die 12 out of which the plastic extrudate is expelled in belt form. While still in the plastic state, the extrudate 13 reaches the shaping means 20 which, in the present case, is formed by two counter-rotating calender rolls 21, 23. Depressions 22 and 24, whose shape in each case corresponds to one half of the tablet to be produced, are formed in the surfaces of the rolls. The rolls are mutually adjusted so that in each case two halves of the shape coincide exactly in the contact region. In this contact region the rolls form an intake slit 25, which extrudate 13 enters and is compressed to a tablet belt 14.

The tablet belt produced in this way is depicted in more detail in Figures 2 and 3. The tablets 15 in the tablet belt 14 are connected together by product webs 16. As is evident in particular from the sectional depiction in Figure 3, the product webs 16 are very thin compared with the tablets 15.

The tablet belt reaches, where appropriate via suitable deflecting devices 17, a first transport means 30 which, in the present case, is designed as belt conveyor unit. The conveyor unit has a circulating conveyor belt 31 and two deflecting rolls 32, 33. In the example depicted there is also provision of cooling means 70, with depiction by way of example of a circulating air cooling 71 with a cooling unit 72 above the tablet belt 14 and cooling plates 73 below the tablet belt 14.

The length of the conveyor belt 31 is chosen - depending on the additional cooling means used - so that at the end of the conveyor belt the product webs 16 have cooled so much that they already have a certain brittleness. The substantially solidified tablet belt on the transport means 30 defines a transport plane 34 - depicted by a broken line in Figure 1.

The singulating means 40 immediately follows the first transport means 30 and consists in the present case of two rollers 41, 42 pressed against one another. The upper roller 41 is designed as embossed roller, while the lower roller is designed as smooth roller. The rollers are displaced slightly relative to one another in the direction of transport of the belt and are, moreover, arranged so that the slit 43 defined by the rollers is located below the transport plane 34 of the solidified belt. It is evident that the tangential plane 44 - depicted by a broken line - of the slit 43 forms an angle with the transport plane 34,

so that it is clear that the solidified band is diverted downward on being guided through the slit 43. This diversion exerts a force essentially perpendicular to the plane of the tablet belt 14, which causes the thin product webs 16 to break. In the example depicted, there is also a guide device 45 provided for the tablet belt between the two rollers 41 and 42 and the end of the conveyor belt 31.

After passing through the singulating means, the tablets of the belt are in the form of single tablets 18, some of which still have residues of the product web on the periphery. The individual tablets 18 fall onto a second transport means 16, which is designed in this case as a shaking screen 61. The shaking screen 61 guides the individual tablets 18 into the deflashing means 50, which consists of a rotating drum 52 with inlet opening 51. During transport on the shaking screen 61, the residues of the product webs are broken off the individual tablets 18 and enter a collecting channel 62. The flash present on the tablets is therefore now only very thin and is completely abraded off after a short treatment time in the drum 52.

Figure 4 shows another variant of the roller combination of the invention for the singulating means 40. The roller 46 rotating above the tablet belt has longitudinal bars 47, while the lower roller 48 has transverse bars 49 which are arranged essentially perpendicular to the longitudinal bars 47.

Figure 5, finally, shows another variant of a breaking roller for the singulating means 40'. The roller 46' has a plurality of flexible thin plastic plates 47' oriented along the axis of the roller 46'. The thin plates may be, for example, bonded or molded onto the basic cylindrical element of the roller, or be secured in slots formed therein. The thin plate roller 46' can be employed as single breaking roller or together with a counter-roller of similar construction or a smooth roller.

The term "tablet" is intended for the purpose of the present invention to have the widest possible meaning. It is linked neither to a particular shape nor to a particular application. It therefore encompasses, for example, tablets for oral use, but also tablets for example for rectal use in the form of suppositories. In this connection, tablets also mean all dosage forms suitable for use as pharmaceuticals, crop treatment compositions, and human and animal foodstuffs, and for releasing fragrances and perfume oils.

Active pharmaceutical ingredients for the purpose of the invention mean all substances with a pharmaceutical action and minimal side effects as long as they do not decompose under the processing conditions. The amount of active ingredient per dose unit and the concentration may vary within wide limits depending on the efficacy and rate of release. The only condition in this connection is that they suffice to achieve their desired effect. Thus, the active ingredient concentration can be in the range from 0.1 to 95, preferably from 20 to 80, in particular from 30 to 70, percent by weight. The term active ingredient also encompasses in the present connection any combinations of active ingredients. Vitamins, for example, as also active ingredients for a purpose of the invention. Particularly preferred active ingredients are ibuprofen (as racemate, enantiomer or enriched enantiomer), ketoprofen, flurbiprofen, acetylsalicylic acid, verapamil, paracetamol, nifedipine and captopril.

The polymeric binder must soften or melt in the complete mixture of all the components in the range from 50 to 180°C, preferably 60 to 130°C. The glass transition temperature of the mixture must therefore be below 180°C, preferably below 130°C. If necessary, it is reduced by conventional, pharmacologically acceptable plasticizing excipients. Suitable polymeric binders are described, for example, in WO 97/15291.

Polymeric binders preferably employed for the melt extrusion of active pharmaceutical ingredients are: polymers or copolymers of N-vinylpyrrolidone, Eudragit types (acrylic resins) or celluloses. Particular preference is given in this connection to: polyvinylpyrrolidone (PVP), copolymers of N-vinylpyrrolidone and vinyl esters such as vinyl acetate, poly(hydroxyalkyl acrylates), poly(hydroxyalkyl methacrylates), polyacrylates, polymethacrylates, alkylcelluloses or hydroxyalkylcelluloses.

The extrudable mixture may, besides the polymeric binder and the active ingredient(s), also contain conventional additives, for example plasticizers, lubricants, flow regulators, dyes, stabilizers or wetting agents, preservatives, disintegrants, adsorbents, mold release agents and blowing agents. It is likewise possible for conventional pharmaceutical excipients, for example extenders and fillers, to be present. Suitable additives and pharmaceutical excipients are described, for example, in WO 97/15291.

Examples

Comparative example 1

A mixture containing 48% by weight of verapamil hydrochloride as active ingredient and hydroxypropylcellulose, methylhydroxypropylcellulose and lecithin powder as excipients was processed in a twin screw extruder (ZSK-58; Werner und Pfleiderer) to a homogeneous melt. The melt throughput was 120 kg/h. The material temperature shortly before the die of the extruder was about 120-130°C. The melt was discharged through a slot die in the form of a sheet and shaped in a downstream molding roll calender to elongate tablets (without score, about 20 mm long, about 5 mm thick). The tablets left the calender in the form of a coherent tablet belt. The tablet belts cooled on a transport belt with a total length of about 4 m through radiation of heat to the surrounding air.

At the end of the transport belt, 50 kg of the resulting tablet belt were broken down manually into smaller pieces of belt which were then introduced into a Driacoater pan (from Driam). The singulation and deflashing took place with the drum rotating at 20 rpm. The entire process took about 40 minutes. It was possible to singulate and deflash all the tablets.

Comparative example 2

The test took place as indicated in comparative example 1, but the calendering resulted in elongate tablets (identical length/width) with a score in the middle of the tablet. The singulation and deflashing in the Driacoater resulted in about 10-30% of the tablets being broken even during the rotation in the Driacoater.

Example 1

The test took place as indicated in comparative example 1, but with the following alterations:

- The transport belt contained at the end a brush roller (diameter about 9 cm) which was driven by a separate driving motor. The speed of rotation of the breaking rollers was adjusted to suit the conveying speed of the transport belt.

- The calendering resulted in breakable tablets having a score in the middle (score geometry as in comparative example 2).

Satisfactory singulation of the tablet belts was possible with the aid of the brush rollers. 50 kg of the singulated tablets were then put in a Driacoater and deflashed with the drum rotating at 5-10 rpm. Deflashing was complete after only 10 minutes. There was no detectable increase in the proportion of broken tablets.

Example 2

The test took place as indicated in example 1, but in place of a brush roller at the end of the transport belt there was a plastic roller 450 mm long with 9 thin plates oriented in the long axis of the roller (corresponding to the depiction in figure 5). The basic element of the cylindrical roller, which consisted of POM, had a diameter of 75 mm. The thin plates were made of flexible PVC, were inserted about 15 mm deep into the roller element and projected about 20 mm beyond the surface of the roller.

Satisfactory singulation of the belts of tablets with scores was possible with the aid of the thin plate rollers. 400 kg of the singulated tablets were then put in a Driacoater and deflashed with the drum rotating at 5-10 rpm. Once again, there was no detectable increase in the proportion of broken tablets.

We claim:

1. A process for producing tablets by melt extrusion, in which an extrudable mixture is heated and extruded in the form of a continuous product strip, the still deformable product strip is compressed to a continuous tablet belt, the individual tablets in the belt being connected together by product webs, the tablet belt is allowed to cool, and the tablets are finally singulated and deflashed, wherein firstly the tablets are mechanically singulated in a continuous process, and then the singulated tablets are transported further and subsequently deflashed.

2. A process as claimed in claim 1, wherein a force with a component perpendicular to the plane of the tablet belt is allowed to act on the tablet belt for singulation of the tablets.

3. A process as claimed in either of claims 1 or 2, wherein a force with a component parallel to the plane of the tablet belt is allowed to act on the tablet belt for singulation of the tablets.

4. A process as claimed in either of claims 2 or 3, wherein the perpendicular force component is generated by diverting the solidified tablet belt out of its transport plane.

5. A process as claimed in either of claims 3 or 4, wherein the parallel force component is generated by exerting a traction force on the solidified tablet belt.

6. An apparatus for producing tablets, in particular for carrying out the process as claimed in any of claims 1 to 5, having at least one extruder (10), having means (20), downstream of the extruder, for shaping a tablet belt (14), having first transport means (30), downstream of the shaping means (20), for the tablet belt (14) and having means (40, 50) for singulating and deflashing the tablets, wherein the means for singulating and deflashing the tablets comprise at least one singulating means (40), downstream of the first transport means (30), and at least one deflashing means (50), downstream of the singulating means and spatially separate therefrom.

7. An apparatus as claimed in claim 6, wherein the singulating means (40) comprises at least one rotatable roller (41) for diverting the tablet belt (14) out of a transport plane (34) of the first transport means (30).

8. An apparatus as claimed in claim 7, wherein the singulating means (40) comprises two counter-rotating rollers (41, 42) which can be pressed against one another.

9. An apparatus as claimed in any of claims 6 to 8, wherein the singulating means (40) comprises at least one brush roller or embossed roller (41).

10. An apparatus as claimed in any of claims 6 to 9, wherein the first transport means (30) comprises means (70) for cooling the extruded tablet belt.

11. An apparatus as claimed in any of claims 6 to 10, wherein a second transport means (60) is provided between the singulating means (40) and the deflashing means (50) and comprises a shaking or vibrating unit (61).

Abstract

The invention relates to a process and an apparatus for producing tablets by a melt extrusion, having an extruder (10) and molding rolls (21, 23) for producing a continuous tablet belt (14), with means being provided for singulation and deflashing the cooled extruder tablet belt (14), which consist of breaking rollers (40) for singulating the tablets and of deflashing means (50) downstream of the breaking rollers and spatially separate therefrom, for example a rotating coating pan.

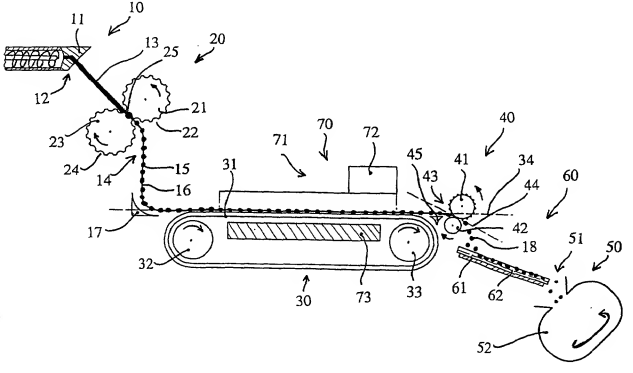

Figure for abstract

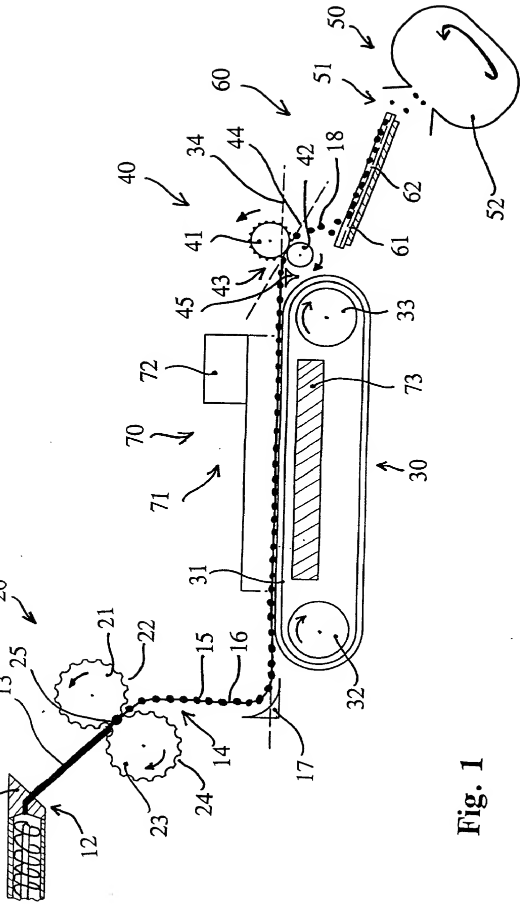
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Fig. 1

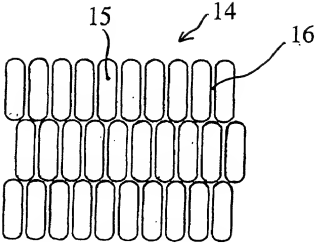

Fig. 2

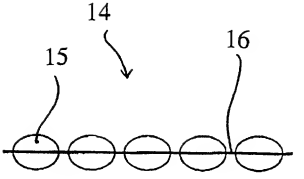

Fig. 3

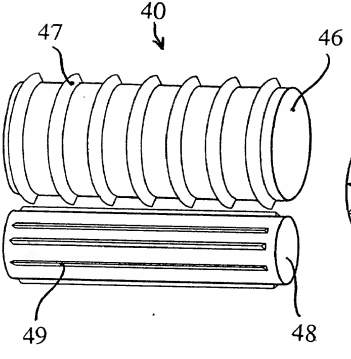

Fig. 4

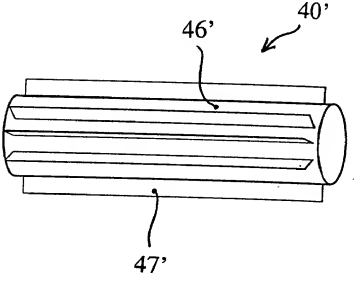

Fig. 5

Declaration, Power of Attorney

We (I), the undersigned inventor(s), hereby declare(s) that:

My residence, post office address and citizenship are as stated below next to my name,

We (I) believe that we are (I am) the original, first, and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled

Method and device for producing tablets

the specification of which

[✓] is attached hereto.

[ ] was filed on _____ as

Application Serial No. _____

and amended on _____.

[x] was filed as PCT international application

Number PCT/EP 99/ 06672

on September 9, 1999

and was amended under PCT Article 19

on _____ (if applicable).

We (I) hereby state that we (I) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

We (I) acknowledge the duty to disclose information known to be material to the patentability of this application as defined in Section 1.56 of Title 37 Code of Federal Regulations.

We (I) hereby claim foreign priority benefits under 35 U.S.C. § 119(a)–(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed. Prior Foreign Application(s)

Application No.	Country	Day/Month/Year	Priority Claimed
19841244.4	*Germany*	*09 September 1998*	[x] Yes [ ] No

pdusdpoa01 - 25

We (I) hereby claim the benefit under Title 35, United States Codes, § 119(e) of any United States provisional application(s) listed below.

(Application Number)	(Filing Date)
(Application Number)	(Filing Date)

We (I) hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

Application Serial No.	**Filing Date**	**Status (pending, patented, abandoned)**

And we (I) hereby appoint **Messrs. HERBERT. B. KEIL**, Registration Number 18,967; and **RUSSEL E. WEINKAUF**, Registration Number 18, 495; the address of both being Messrs. Keil & Weinkauf, 1101 Connecticut Ave., N.W., Washington, D.C. 20036 (telephone 202–659–0100), our attorneys, with full power of substitution and revocation, to prosecute this application, to make alterations and amendments therein, to sign the drawings, to receive the patent, and to transact all business in the Patent Office connected therewith.

We (I) declare that all statements made herein of our (my) own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

pfdatpco001 - 25

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